A PULSAR Phase 3 Trial *Post-hoc* Analysis: Evaluating the Timing and Magnitude of Control of Disease Activity with Aflibercept 8 mg and Faricimab, Applying Similar Disease Activity Criteria Across Different Pivotal Phase 3 Trials for nAMD

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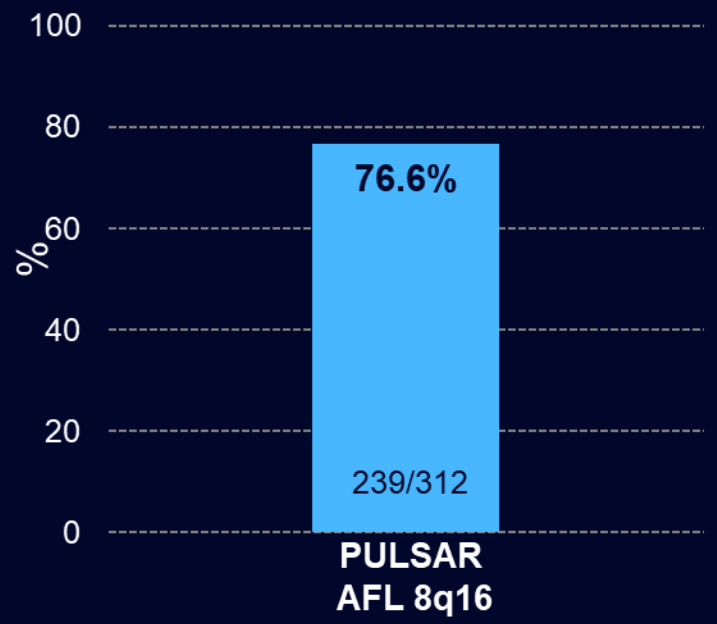
Background and Aims

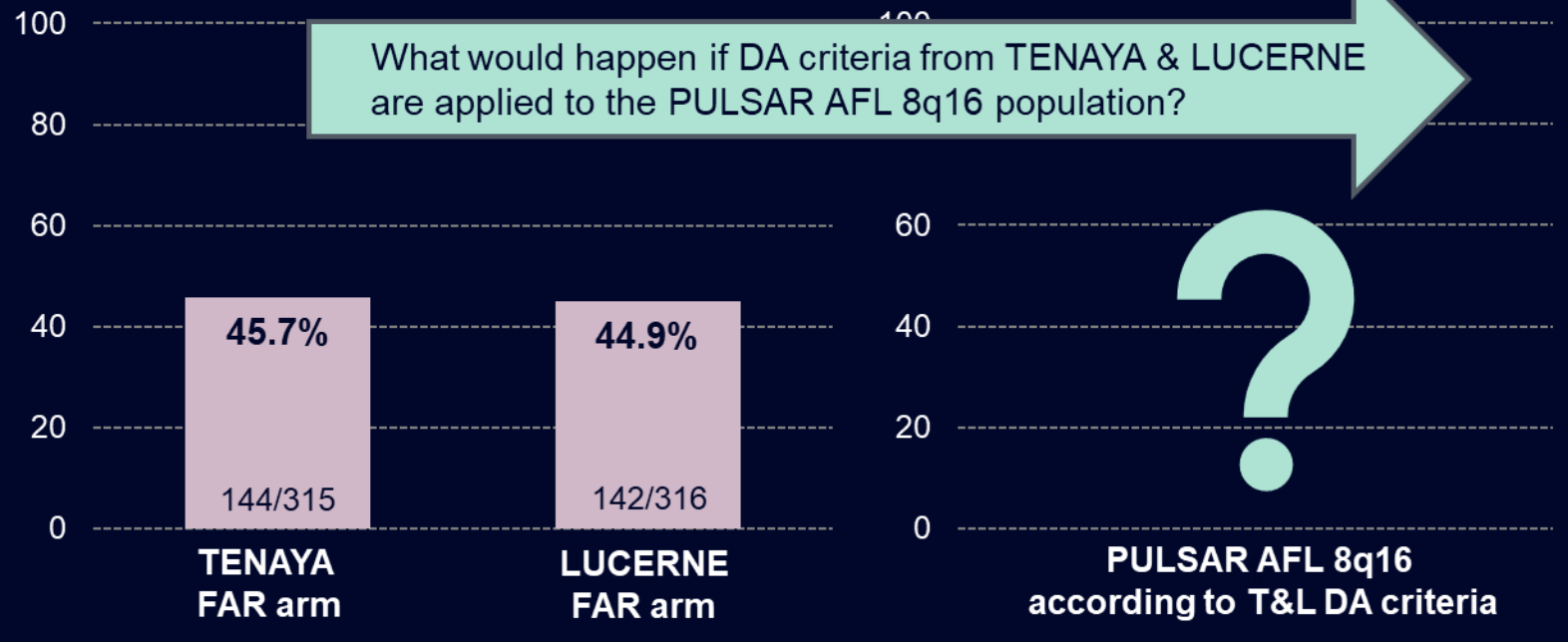
PULSAR, and **TENAYA & LUCERNE**, were studies using anti-VEGF therapies with **presumed different** durability, and with **different** treatment algorithms and criteria for interval modification

PULSAR N=1009	Aflibercept 8 mg (8q12/8q16) vs aflibercept 2 mg (2q8) for treatment-naïve nAMD[1]
TENAYA & LUCERNE N=1329	Faricimab 6 mg (up to q16) vs aflibercept 2 mg (2q8) for treatment-naïve nAMD[2]

Proportion of **Patients** Maintaining q16 Dosing Through Week 48 (%)[1]



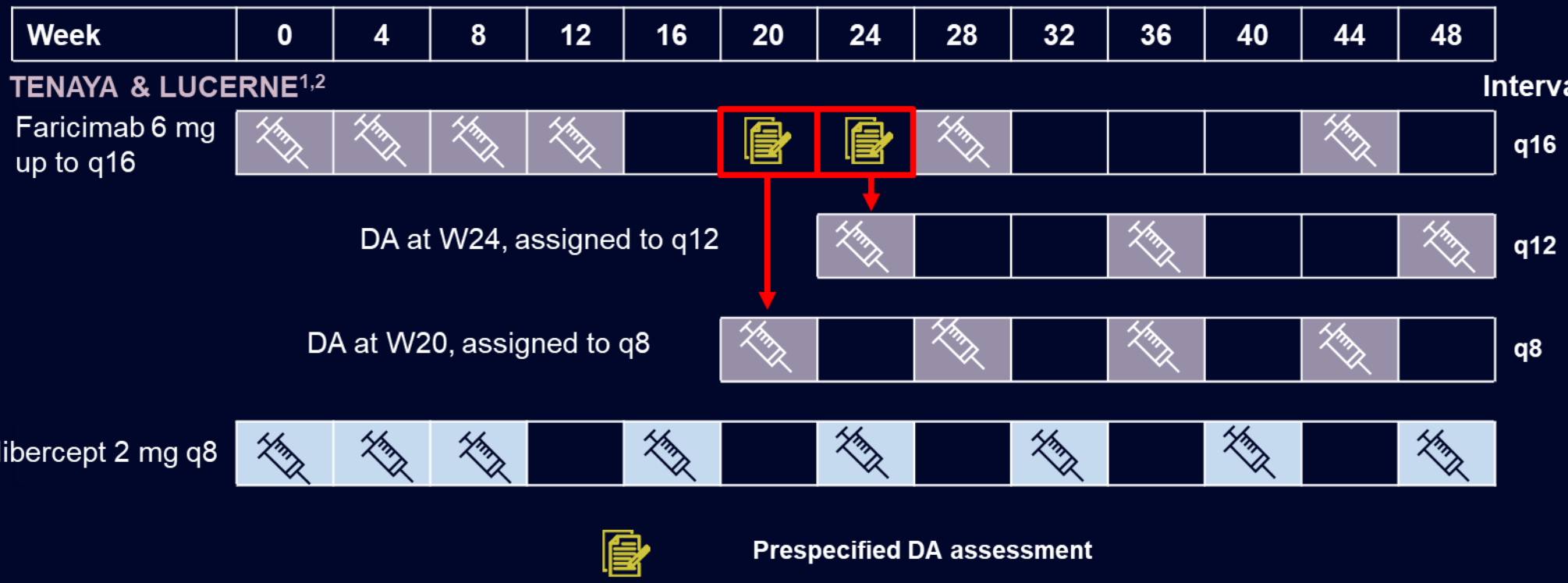
Proportion of **Patients** assigned to q16 Dosing Through Week 48 (%)[2]



2q8, aflibercept 2 mg every 8 weeks; **8q12/8q16**, aflibercept 8 mg every 12/16 weeks; AFL, aflibercept; **anti-VEGF**, anti-vascular endothelial growth factor; **DA**, disease activity; **FAR**, faricimab; **nAMD**, neovascular age-related macular degeneration; **q16**, every 16 weeks; T&L, TENAYA & LUCERNE. 1. Lanzetta P, et al. Lancet. 2024;403:1141–1152. 2. Heier J. et al. Lancet. 2022;399:729–740.

TENAYA & LUCERNE Study Design

pulsar nAMD



Prespecified DA assessment

CST increase

>50 µm (vs average CST over previous 2 scheduled visits)

or

≥75 µm (vs lowest CST at either of previous 2 scheduled visits)

BCVA loss[a]

or

≥5 letters (vs average BCVA over previous 2 scheduled visits)

or

≥10 letters (vs highest BCVA at either of previous 2 scheduled visits)

or

New macular hemorrhage (per the investigator and attributable to nAMD)

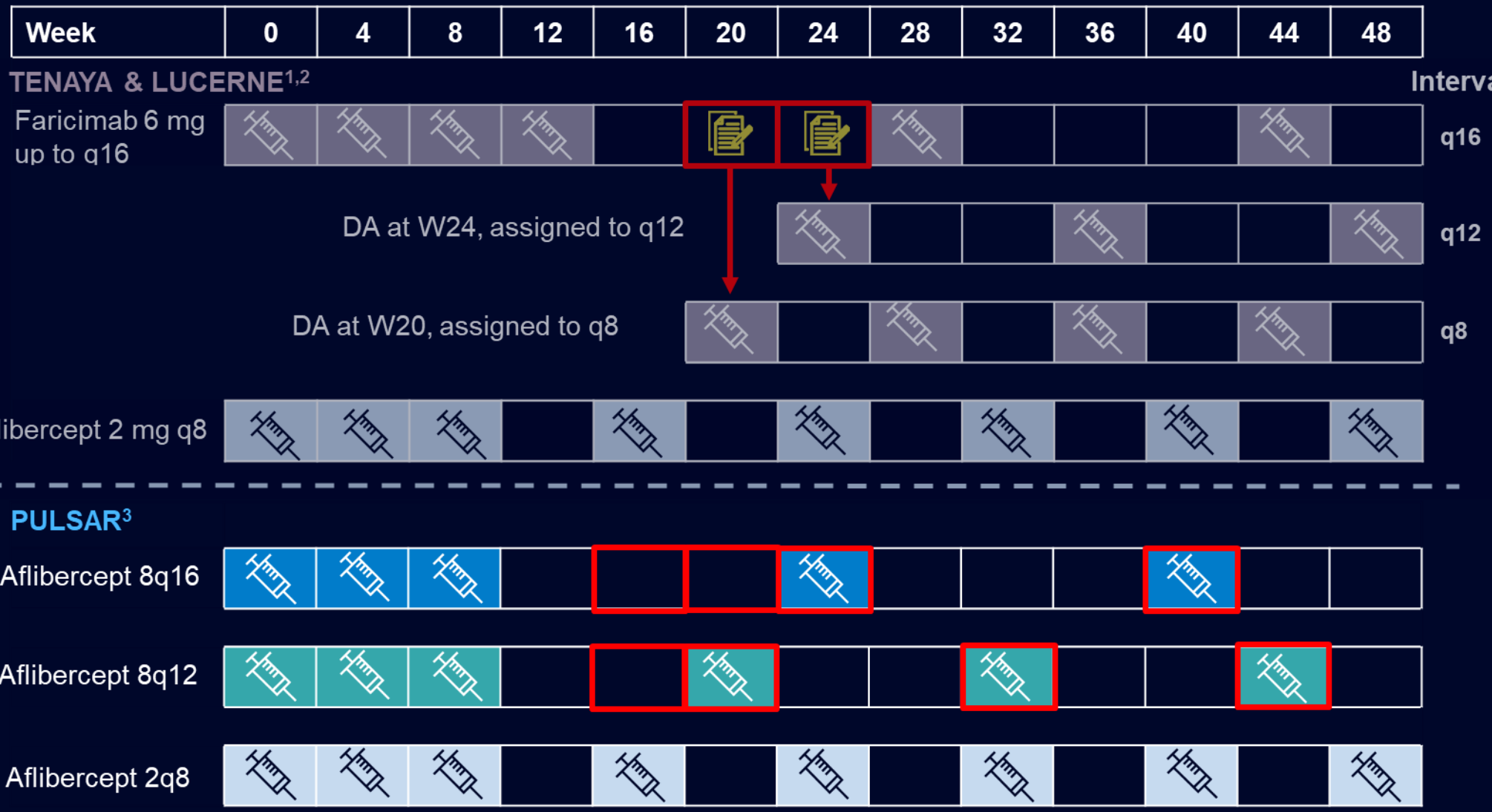
or

Significant nAMD disease activity requiring immediate treatment (per the investigator)[b]

Representations of study design have been simplified, please refer to original publications for more information. In TENAYA & LUCERNE, sham injections given to mask treatment intervals (i.e., at every visit if not receiving study treatment). [a]Owing to nAMD DA. [b]Applicable to Week 24 only. **BCVA,** best-corrected visual acuity; **CST**, central subfield thickness; **q8/q12/q16,** every 8/12/16 weeks. 1. Khanani A. et al. Ophthalmol Sci. 2021:17;100076. 2. Heier J. et al. Lancet. 2022;399:729–740.

TENAYA & LUCERNE, and PULSAR, Study Design

pulsar nAMD



Note: Difference in the number of opportunities for interval adjustment

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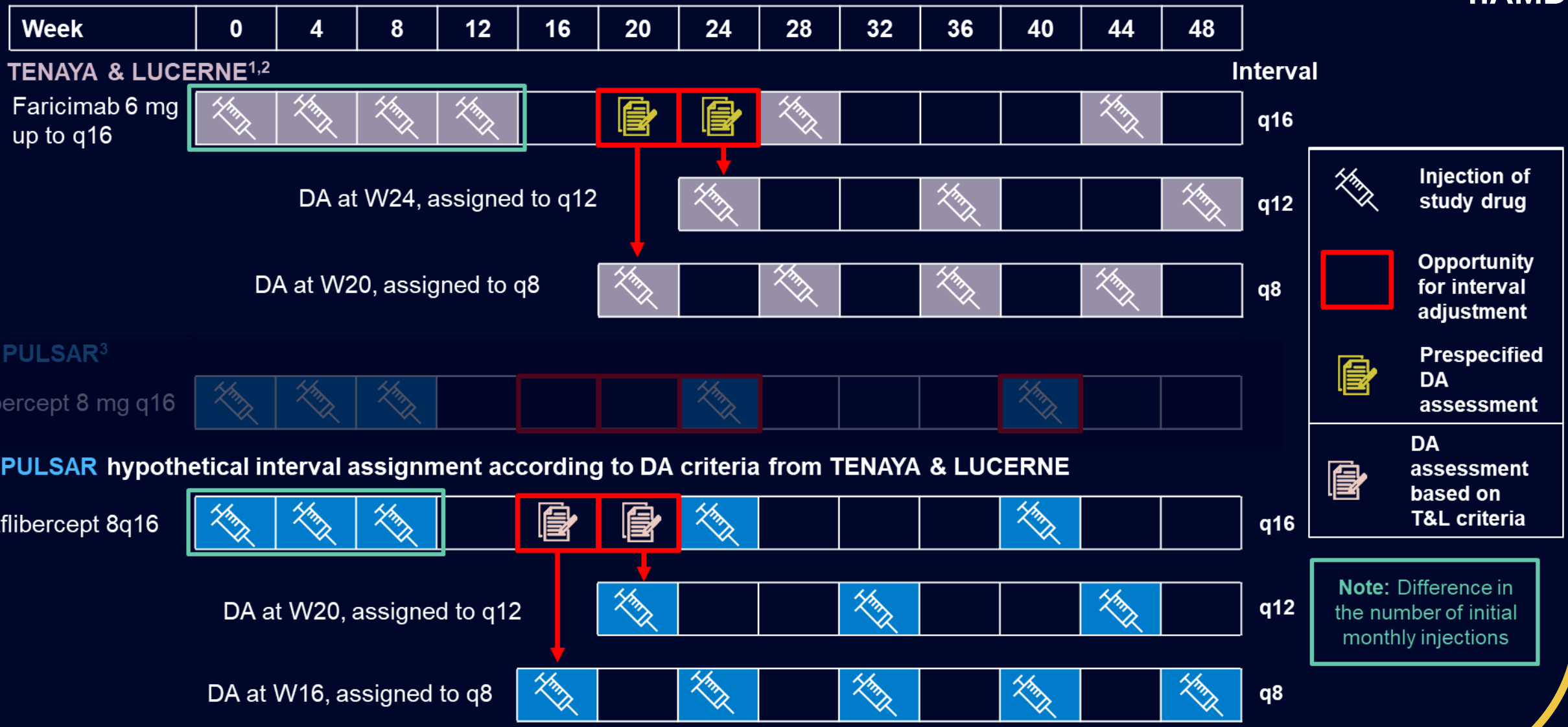
Application of TENAYA & LUCERNE DA Criteria to PULSAR 8q16 Population

pulsar nAMD



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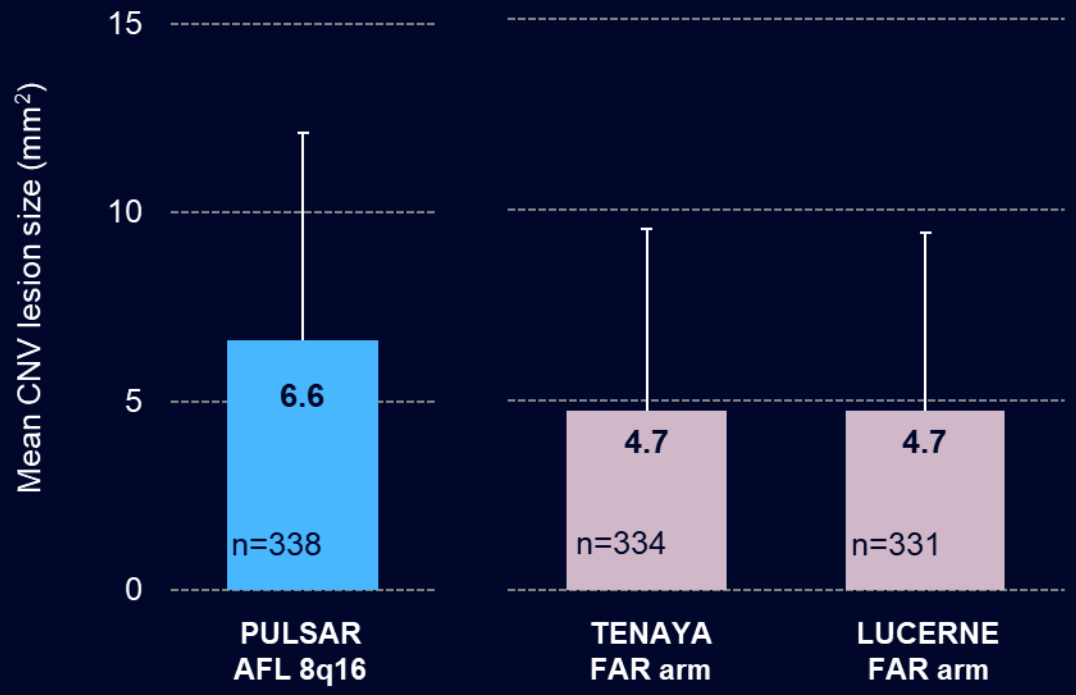
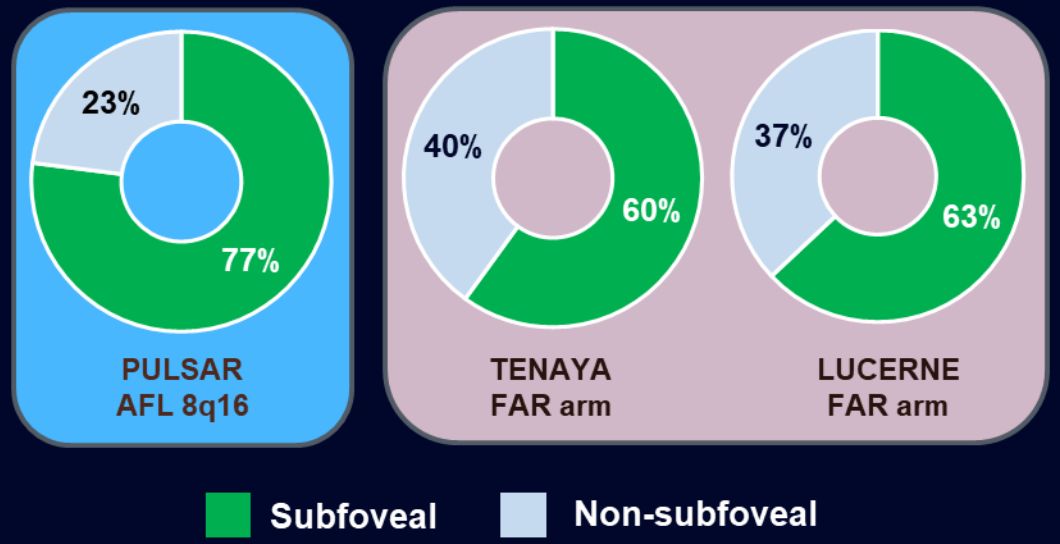
Baseline Characteristics of Patients in PULSAR[1] and TENAYA & LUCERNE[2]

pulsar nAMD

Baseline CNV lesion size



CNV Location (%)



A conservative approach was used in this analysis

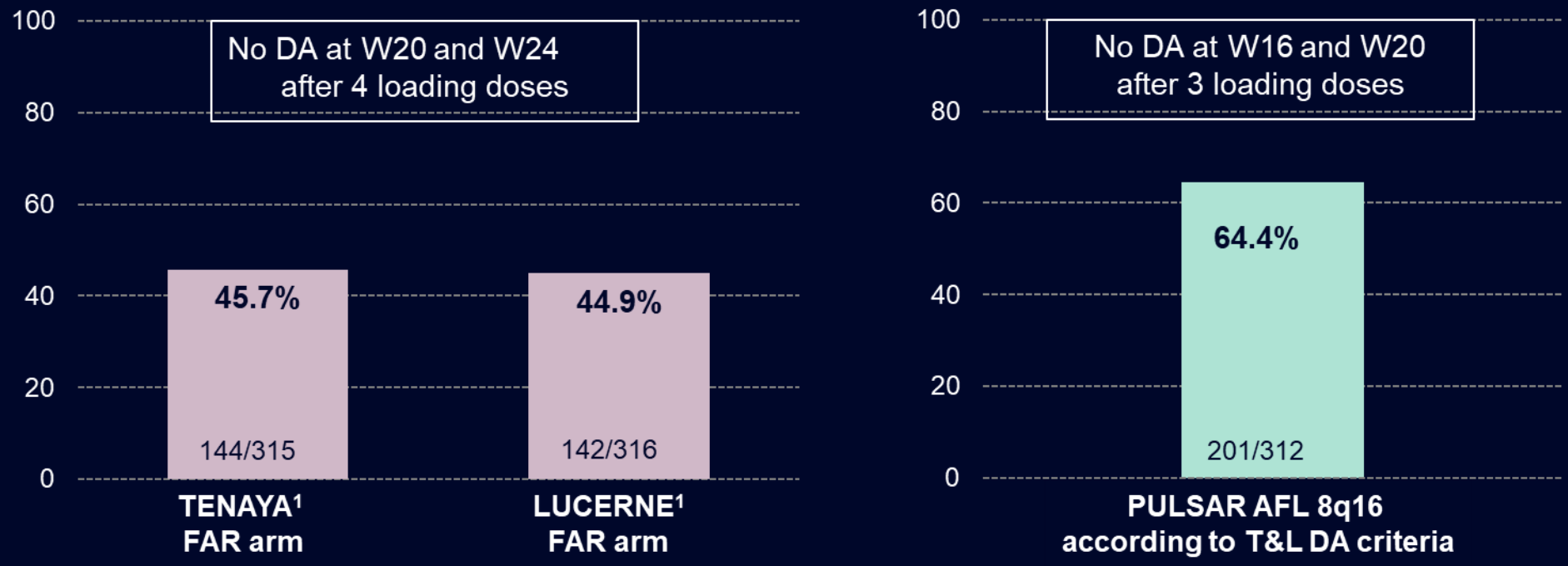
- Different magnitude of disease activity at baseline was observed in different studies
- No adjustments were made to compensate for **fewer initial monthly doses**, **larger lesion size**, or **higher proportion of subfoveal CNV** in **PULSAR**, even though these could increase the difficulty for **aflibercept 8mg** to achieve control of disease activity

Error bars indicate SD. **CNV**, choroidal neovascularization; **CRT**, central retinal subfield thickness; **ETDRS**, Early Treatment Diabetic Retinopathy Score; **SD**, standard deviation. 1. Lanzetta P, et al. Lancet. 2024;403:1141–1152. 2. Heier J. et al. Lancet. 2022;399:729–740.

Proportion of Patients Assigned to Aflibercept 8q16 Treatment Through W48 should TENAYA & LUCERNE DA Criteria be Applied

pulsar nAMD

Proportion of **Patients** assigned to q16 Dosing Through Week 48 (%)



When DA criteria from TENAYA & LUCERNE are applied:

- **64%** of patients in the **aflibercept 8q16 group in PULSAR** are predicted to have no DA at W16 or W20 (and thus would be assigned to q16 dosing intervals through W48)
- This compares to **~45%** of patient receiving **faricimab** in **TENAYA & LUCERNE**, with no DA at W20 and W24

Conclusions

pulsar
nAMD

Findings from this *post-hoc* analysis support earlier control of disease activity with aflibercept 8 mg in PULSAR (64% at W16/W20) than that reported for faricimab in TENAYA and LUCERNE (45% at W20/W24),[1] using similar DA assessment criteria

Inter-trial assessments should be interpreted with caution due to various **limitations**, such as **differences in magnitude of baseline DA and impact of DA criteria on study protocols**

In this *post-hoc* analysis, limitations include the **differences in the number of initial monthly injections and baseline disease activity between PULSAR and TENAYA & LUCERNE**

Despite the **conservative approach** applied, these results should be **interpreted with caution**

1. Heier J. et al. Lancet. 2022;399:729–740.